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| APPLICATION NO. | F | ILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------------------|--------------------|------------|----------------------|---------------------|------------------|
| 09/673,735 | 673,735 12/27/2000 | | Bernd Dorken | 028622/0102 | 3749 |
| 22428 | 7590 | 04/12/2005 | | EXAM | INER |
| FOLEY AND LARDNER SUITE 500 | | | | HELMS, LARI | RY RONALD |
| 3000 K STREET NW | | | | ART UNIT | PAPER NUMBER |
| WASHINGTON, DC 20007 | | | | 1642 | |

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief

| Application No. | Applicant(s) | |
|-----------------|---------------|--|
| 09/673,735 | DORKEN ET AL. | |
| Examiner | Art Unit | |
| Larry R. Helms | 1642 | |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --THE REPLY FILED 28 March 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. 1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods: a) The period for reply expires months from the mailing date of the final rejection. b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f). Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1,704(b). NOTICE OF APPEAL 2. The Notice of Appeal was filed on 28 March 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a). **AMENDMENTS** 3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because (a) They raise new issues that would require further consideration and/or search (see NOTE below); (b) They raise the issue of new matter (see NOTE below); (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or (d) They present additional claims without canceling a corresponding number of finally rejected claims. NOTE: . (See 37 CFR 1.116 and 41.33(a)). 4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324). 5. Applicant's reply has overcome the following rejection(s): ___ 6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s). 7. Tor purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended. The status of the claim(s) is (or will be) as follows: Claim(s) allowed: none. Claim(s) objected to: none. Claim(s) rejected: 1-5,7-16,20-23,30,33 and 35-45. Claim(s) withdrawn from consideration: AFFIDAVIT OR OTHER EVIDENCE 8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e). 9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1). 10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached. REQUEST FOR RECONSIDERATION/OTHER 11.

The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet. 12. Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 13. Other: See Continuation Sheet. LARRY R. HE "S. PH.D PRIMARY ExaminER

Continuation of 11. does NOT place the application in condition for allowance because: the 112 firest rejection is maintained because although the claims require binding as stated in the response, the specification as well as the prior art does not teach an antibody with only one CDR that binds. The 103 rejection is maintained. The response states that Bohlen needed anti-CD28 antibodies with his molecule (see page 12 of response). In response to this Bohlen et al teach a bispecific molecule directed to the antigens claims, regardless of any additional molecules. The difference is that Bohlens molecule is not a single chain. The response states that Kipriyonov's molecules which were made like Gruber did not function and Kipriyanov's studies after Mack would provide evidence to not pursue a single chain antibody (see page 14 of response). In response to this argument, the art of Kipriyanov (int J cancer 77:763-772, 1998) is not prior art because it was published after the effective filing date of the application. The art of Mack teaches a bispecific single chain antibody in the orientation claimed and it was functional. Therefore one reading Mack would conclude that the orientation is essential and would pick the orientation claimed.

Continuation of 13. Other: the IDS filed 3/28/05 will not be considered because it is not in compliance. It was filed after the final rejection and does not contain certification.

LARRY R. HELMS, PH.L PRIMARY EXAMINER